susception is of great diagnostic value, is not met with so often in acute cases in the adult. Leichenstein found a tumor present in about 50 per cent. of all cases in all ages. It is most frequently met with in the cecal and ileocolic varieties. In none of our cases was a tumor demonstrable. When present it may be discovered through the abdominal walls or in the rectum. It varies in size with the size of the intussusception, but never gives an idea of the actual amount of bowel invaginated. It is usually hard and resisting. It is also usually more prominent during attacks of pain and sometimes has a distinct range of motion.

The temperature, as a rule, remains normal or slightly above normal, except in cases associated with shock. Collapse, however, is far less common than in obstruction due to bands. It is far more common in young infants and is then rarely fatal. Tenesmus in acute and subacute attacks is a severe, early, and constant symptom. The nearer the invagination is to the anus the severer the tenesmus. It may or may not be associated with blood or blood-stained mucus. Thirst in intestinal obstruction depends upon the degree of vomiting, hence is less marked in intussusception than other forms of strangulation.

We believe that operation is the safest and most logical procedure in the treatment of acute intussusception. To have the best results early diagnosis and prompt action are essential. Any attempt to reduce a well-defined intussusception by the use of forced enemas is in our opinion losing valuable time.

PRIMARY CARCINOMA OF THE URINARY BLADDER.

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(From the Pathological Laboratory of Rush Medical College, University of Chicago.)

A review of the literature has failed to reveal a recent report of any considerable series of cases of primary carcinoma of the bladder thoroughly studied from both the clinical and the anatomical sides. Going back a few years there is no lack of material from which to draw, and it is from this source that most of our literature is derived. The marked discrepancies in the statistics and in the statements of the various authors would lead one to infer that most of the original literature will not bear a very close inspection, and this is to a certain extent borne out by the facts. Carcinoma of the bladder is a hidden disease. One cannot note its beginning and watch its progress from day to day. Furthermore, its location and malignant nature make its clinical manifestations peculiarly subject to confusion with those of complicating or neighboring diseases. Such being the case, it is very evident that statistics gleaned from the records of the clinician and the surgeon may be very inaccurate, and the inferences based thereon no safe guide. On the other hand, the conclusions of the pathologist and the microscopist, widely at variance with those of the practitioner, need comparison with the reports of the latter.

The above considerations have furnished me with the excuse for the report of the following series of 10 cases, the records and specimens of which are in the pathological laboratory of Rush Medical College. I wish to emphasize the fact that the report is based primarily upon postmortem examinations, supplemented in each case by a careful microscopic examination, and as far as possible, by the clinical data. In each instance the following questions were answered in the affirmative: (1) Is the tumor malignant? (2) Is it a carcinoma? (3) Is it primary in the bladder?

The ultimate standard of malignancy was that set by Ziegler; namely, infiltration of the bladder wall or the formation of metastases. Parenchymatous infiltration of the muscularis was demonstrable, microscopically, in every case; the epithelial character of the tumor was established by the histological appearance; and, without exception, we were able to exclude the possibility of prostatic or other extravesical origin.

CASE I.—A man, aged thirty-nine years. The clinical history was not to be obtained. At the autopsy was found: "a condition of right pyonephrosis and left hydronephrosis; the left ureter is dilated to the size of a lead pencil. The bladder contains a grayish-brown, purulent fluid. The inner wall is studded with nodules, varying in size from that of a split pea to a walnut. The prostatic urethra is invaded and a tumor, situated on the trigone, obstructs the ureters." A study of microscopic sections showed the growths to be papillary carcinomas with extensive necrosis, and with finger-like projections extending down into the muscular wall.

CASE II.[1]—J. S., male, aged forty-six years, a musician, was first admitted to the Presbyterian Hospital in the summer of 1901, complaining of pain and strangury on urination. At that time a diagnosis of cystitis was made. After his discharge the patient's symptoms increased in severity and he lost flesh. He developed an irregular fever with occasional chills. He returned to the hospital, and was operated on March 26, 1902, a suprapubic incision and perineal drainage being performed. Several small calculi were removed from the bladder, and a diagnosis of carcinoma was made from the scrapings. Two days later a blood examination showed a rather marked anemia with a color index of 0.6, and a leukocytosis of 18,600. The urine was acid until a few weeks before death, when it became alkaline. Death occurred April 30.

The postmortem examination showed a secondary involvement of the retroperitoneal, pelvic, and mesenteric lymph glands and growths in the lungs and liver. In addition there was an ascending cysto-uretero-pyelonephritis with dilatation of the ureters and renal pelves on both sides. The entire inner surface of the bladder wall, including the urethral and both ureteral orifices, was invaded by tumor tissue, which projected in large, necrotic masses and showed extensive ulceration. The anterior wall was adherent to a subperitoneal carcinomatous mass and was torn in separating the organ from the symphysis. A perforation appeared to have taken place at that point and to have been walled off by adhesions. Microscopic examination showed that the growth was what may be described as a pseudotubular carcinoma, the cells being, for the most part, arranged in solid cords and nests, but showing in places the appearance of imperfect tubules. The muscular wall was extensively infiltrated.

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[1] Reported in Trans. Chicago Path. Soc., 1902, v, 105.

CASE III.—H. K., male, aged forty-four years, was admitted to the Norwegian Tabitha Hospital. The patient gave a history of gonorrhœa at twenty-two years. This was closely followed by strictures, cystitis, and pyelonephritis. Two years later a urethrotomy was performed, after which he enjoyed good health until the spring of 1901. At that time urination became frequent and painful. In January, 1902, he fell on his right hip. Two months later a small, hard tumor developed in the reigon of the right sacro-iliac joint, the urinary symptoms in the meantime growing progressively worse. An operation was performed for the removal of this osteal tumor on May 5. The patient developed an irregular fever after the operation and died May 27, 1902. The urine was acid throughout and contained a large amount of albumin and numerous pus cells.

The autopsy revealed: "A carcinoma of the bladder with metastases in the right iliac bone, left eighth rib, right second and ninth ribs, liver, mesenteric, retroperitoneal, inguinal, and peribronchial lymph glands. Two of the affected ribs have become fractured. There is an ascending pyelonephrosis with dilatation of the right ureter and renal pelvis, and also a psoas abscess. The bladder contains a large amount of gravel glued together with mucus and adherent to the mucosa in the form of balls. The tumor, as a diffuse thickening of the bladder wall with projecting ridges 1 or 2 cm. in width at the base, occupies almost the entire lower one-third of the bladder and extends up on the right wall. Both ureteral orifices are involved in the tumor mass, the right being completely closed. The projecting point of one of the ridges partly blocks the internal urethral orifice. The prostate is smooth externally and of normal size. The tumor is of rather hard consistency and is not ulcerated." The microscope showed the muscularis to be extensively infiltrated. The sections presented the appearance of a papillary carcinoma, with cords of cells arranged in a glove-like, or arborescent manner.

CASE IV.—O. C., male, aged forty-three years, a farmer by occupation, admitted to the Presbyterian Hospital, gave a history of gonorrhœa nineteen years before his present trouble began. He denied other illnesses. In November, 1901, his first symptoms developed: frequent urination accompanied by a burning sensation. His symptoms grew more severe, he lost weight, and at the time he entered the hospital was having occasional chills accompanied by an irregular fever. There was a slight pyuria and hematuria. The reaction of the urine was alkaline. A blood examination showed the red cells to be 3,912,000; the white cells, 8050; the hemoglobin, 55 per cent. A nephrotomy was performed. The patient survived this operation two weeks, dying November 23, 1902.

The postmortem findings were: "A primary carcinoma of the urinary bladder, with secondary involvement of the kidneys, adrenals, lungs, and left testicle. There is an ascending cysto-uretero-pyelonephritis, and a right perinephric abscess. A stone is impacted in the lower portion of the right ureter; the proximal end of the ureter and the pelvis of the kidney are dilated. There is a slight stricture of the membranous urethra. The external urethral orifice opens at the junction of the glands with the corpus spongiosum." "The upper four-fifths of the bladder wall shows an extremely necrotic, ulcerated, greatly thickened, lining. Superficially the growth is nodular and fungoid. It extends to within 1 cm. of the urethral opening, while the ureters open just below the margin of the tumor mass." The prostate and seminal vesicles were not involved. Microscopically the tumor was found to be a typical papillary carcinoma which had very extensively infiltrated the bladder wall.

CASE V.—H. M., male, aged seventy-two years, was admitted to the Norwegian Tabitha Hospital, to the service of Dr. Sandberg. The family history was negative and the patient denied venereal disease. He had been in good health up to October 15, 1902, when his first symptoms began: severe, lancinating pains in the back and abdomen, radiating to the right thigh and testicle. These continuing, he was admitted to the hospital on November 17. At that time his urine was acid, contained much albumin and numerous red cells. He had no fever. On November 22, about one-half of the bladder, comprising the greater part of the anterior wall, was resected. There was no fever subsequent to the operation, but persistent nausea and vomiting developed, and death supervened December 24.

At the postmortem a considerable necrosis of the bladder wall was found near the operation wound. There was a general, acute, fibrino-hemorrhagic peritonitis, and an acute cystitis and urethritis. Metastatic tumors were found in the liver, lungs, and the right eighth rib, which had sustained a pathological fracture. The ureters and kidneys were practically normal. Quoting from the records, "The left lobe of the prostate is 4 by 2.5 cm. The cut surface is slightly gelatinous; the right lateral lobe answers the same description."

The microscope showed no indication of tumor formation in this organ. Sections of the bladder wall showed that it was deeply infiltrated by tumor cells, evidently those of a papillary carcinoma, of the rapidly-growing type and with a marked tendency to degenerative changes. The secondary tumors were similar to this in character.

CASE VI.—P. J., male, aged thirty-eight years, was admitted to the Presbyterian Hospital to the service of Dr. Robison. No statement as to previous diseases was obtained. The patient was ill in May, 1902, with an affection diagnosticated as "malaria." His urine was bloody and there was frequent and painful micturation. The following winter the hematuria again appeared, and the patient became weak and emaciated. He entered the hospital, and the diagnosis of carcinoma of the bladder was made. Toward the close he developed gastro-intestinal "distress" and a cough. A blood examination showed: red cells, 3,880,000; white cells, 14,800; hemoglobin, 45 per cent.

Only the contents of the abdominal cavity were examined postmortem. Metastatic tumors were found in the liver, mesenteric, and retroperitoneal lymph glands. There was ascites and slight prostatic hypertrophy. A tumor, composed of flat, sessile, soft projecting masses, occupied the inner surface of the posterior wall of the bladder, beginning 3 cm. above the upper border of the prostate and extending to the highest point of the bladder. The tumor showed an extensively ulcerated area and was covered in part by a thick layer of gravel. On microscopic examination both the muscular wall and the serous covering of the bladder were found to be infiltrated with strands and clusters of tumor cells, the arrangement justifying the classification of papillary carcinoma.

CASE VII.—C. E., male, aged sixty-four years, was admitted to the Presbyterian Hospital. This patient, a bricklayer, denied venereal infection, and said that he had used alcoholic drinks in moderation. He gave a history of excellent health up to April, 1903, when urination became difficult, frequent, and painful. On his entrance into the hospital July 16, 1903, his bladder was distended with bloody urine. Rectal examination revealed a prostate the size of a lemon. His temperature was 100.2°. A blood examination showed a red count of 4,670,000; leukocytes, 5200; and hemoglobin, 52 per cent. A prostatectomy was performed July 21. Fever and severe chills followed, and death ensued three days later.

Among the anatomical findings were, "Ulcerative carcinoma of the urinary bladder with secondary involvement of the pelvic and retroperitoneal lymph glands, including a gland at the bifurcation of the aorta." The tissues were all distended by gas generated by the Bacillus capsulatus aërogenes.

Quoting further from the autopsy records, "A large tumor mass measuring 14 by 10 cm., made up of a large number of projecting nodules and partially ulcerated, occupies the whole trigone and the lower part of the bladder. The ureteral papillæ are greatly hypertrophied and project up like horns flattened against the posterior wall of the bladder. About 5 cm. below and a little internal to the right ureteral papilla is a triangular fistula through the tumor mass, entirely perforating the posterior wall of the bladder. The prostate has been removed by operation leaving an opening in the anterior portion of the bladder. In removing the prostate a part of the tumor was also cut away. The ureters are not involved by the tumor down to the point at which they enter the vesical wall. Both ureteral openings into the bladder are greatly stenosed, but not entirely occluded. The left vas can be traced into a tumor nodule lying on the border of the perforation in the posterior wall of the bladder. The left seminal vesicle is apparently surrounded by tumor tissue; the right seminal vesicle is contained in a tumor nodule at the edge of the perforation. The microscopic sections showed such advanced necrosis that it could not be positively determined to which type the carcinoma belonged, the infiltration of the muscularis, however, being very evident.

Case VIII.—Mr. M., aged fifty-six years, a tailor, was admitted to the Presbyterian Hospital. The patient denied venereal disease and gave no other pertinent history. Ten months before death he developed hematuria. Later he complained, in addition to incontinence, of frequent urination with a burning sensation, and of pain in the back. On his entrance into the hospital his urine was neutral in reaction, and contained blood, casts, and much albumin. His symptoms gradually grew worse, he became emaciated and developed a slight fever toward the close.

The postmortem revealed a left suppurative ascending cysto-uretero-pyelonephritis; dilatation of both ureters, with stenosis and kinking of the left. The bladder was occupied by a soft, fungus-like, tumor mass, 9 by 6 cm., which showed extensive necrosis. The tumor was attached to the bladder wall along the right side, the area of attachment beginning above the trigone. The ureteral and urethral orifices were involved only by the pressure of the tumor. There were no metastases and no involvement of neighboring structures. The anatomical diagnosis of papillary carcinoma was verified by the microscope.

Case IX.—J. R. C., male, aged fifty-five years, a sailor by occupation was admitted to Cook County Hospital, November 2, 1906. A history was given of hematuria for seven months. At first there were no other symptoms, but seven weeks before admission pains developed in the region of the bladder with a rapid decrease of weight and strength. On examination the patient's pulse was found to be rapid; and the abdomen below the navel was tense. He was catherized and 500 c.c. of bloody, foul-smelling urine, containing shreds of tissue was drawn off. There is no record of examination of these shreds. The examining-room diagnosis of urinary retention was made. Death occurred three hours later.

The postmortem, held by Dr. Hunter, the Coroner's physician, revealed a carcinomatous growth in the bladder, ascending pyelonephritis, and a right psoas abscess. "There is no involvement of the prostate and no metastatic growths. The tumor, situated on the right anterior part of the bladder wall, forms a hard, slightly ulcerated, almost spherical growth 5 cm. in diameter, projecting into the cavity of the bladder. It is connected to the wall by a pedicle, of softer consistency, 3 cm. in diameter. The muscularis at the site of attachment shows extensive infiltration. The right ureteral orifice as well as the urethral is pressed upon by the tumor." The diagnosis was confirmed by the microscope, the epithelial cells being arranged in several layers about a frame work of branching connective-tissue stroma.

Case X.—J. D., male, aged forty-five years, admitted to the Presbyterian Hospital. The family history was negative. The patient had gonorrhœa at the age of twenty years, and syphilis at twenty-three years, having taken specific treatment for ten years thereafter. In the fall of 1904, after taking cold, he had an attack of severe pelvic pains and frequent urination, lasting for one week. He noticed no further symptoms until six months afterward, when he passed numerous small stones and had two chills. After the removal of eight larger calculi per urethram the concomitant tenesmus and pain subsided; but set in again June 16, 1906, and gradually increased in severity. There had been, however, no hematuria observed and no other abnormal appearances in the urine, except a "ropy substance" during the first attack. Eight weeks before his entrance into the Presbyterian Hospital an operation was performed for vesical calculus and one stone was removed.

Examination on admission showed a vesical fistula. The prostate was enlarged and tender. The urine was alkaline, with a specific gravity of 1010, and contained much albumin, many pus cells, and a few erythrocytes. During the first few days the temperature was irregular, ranging from subnormal to 102°. On October 8, an operation was performed in hopes of removing the tumor. During the next two weeks there were several severe rigors; nausea and diarrhœa developed, and the patient grew gradually weaker, dying November 23.

The pertinent postmortem findings were as follows: "Almost the entire bladder wall above the trigone is diffusely infiltrated by a firm tumor mass, and measures 1 cm. in thickness. From the interior of this part of the bladder extend numerous rounded, oval, and tongue-like projections, the largest being the size of a bean. Both urethral orifices are encroached on by the margin of the tumor. The seminal vesicles and the prostate are not involved. The mucosa of the trigone is dusky, and shows small superficial ulcerations.

There is a condition of double pyonephrosis. Both ureters are markedly distended, measuring, when laid open, from 3 to 5 cm. in circumference. The right ureter contains a stone. On the right side is an accessory ureter extending from the pelvis of the kidney to a point on the ureter 7 cm. above its vesical orifice. Its lumen is patent throughout. The pelves of both kidneys are much dilated and the kidney substance diminished in thickness. In the left kidney several cavities extend from the pelvis into the cortex to within a few millimeters of the surface." There were no metastases. On microscopic examination the tumor proved to be a papillary carcinoma made up of large cuboid cells with vesicular nuclei and a rather scanty stroma.

A good example of the contradictory statements in the literature is met with in regard to the prevailing seat of the tumors. Barling,[2] in an analysis of 260 vesical neoplasms, found two-thirds springing from the base. Albarran[3] divides the bladder into three parts, the lower being below the level of the ureteral orifices. He affirms that most tumors originate in the middle third, and found only 2 out of 88 springing from the trigone; admitting, however, that of tumors originating elsewhere one-third extend to the trigone. On the other hand, Clado,[4] who observed 250 cases of malignant tumor, asserts that their seat of election is the base of the bladder and that extension nearly always takes place in an upward direction, involvement of the rectum, vagina, or prostate rarely taking place, while extension through the muscular wall and intestinal adhesions, consequent on an upward growth, is not at all uncommon.

In our series it could be pretty definitely determined that the seat of origin was in the trigone in three instances. In 1 case (II) it is uncertain whether the tumor had its start in the trigone or in the anterior wall; probably the latter. Three of the tumors showed greatest involvement of the upper part of the bladder while the remainder affected the middle zone more extensively. The urethra was directly involved in the tumor mass in two instances, while in 2 there was partial obstruction by projecting portions of the neoplasms. One or both ureteral orifices were directly implicated in 3 cases, while in 4 others there was partial obstruction by pressure of the tumor or nodules. One tumor (Case VII) had invaded both seminal vesicles, as was demonstrated both by external examination and by serial sections. Of such involvement Clado had not seen an example. None of the growths had extended to the prostate or rectum, and only one had caused perforation into the peritoneal cavity.

As to the frequency of extension to the glands and as to the formation of further metastases there is a wide divergence of opinion. Clado states that of 250 cases of malignant tumor observed in his clinical experience, there were only 4 instances of glandular involvement when the tumor was well localized in the bladder. He also quotes Fere, who in 145 cases found glandular involvement in only 10. Pasteau[5] asserts that the iliac glands are enlarged in 43 per cent. of all sessile and 85 per cent. of all infiltrating tumors, but that metastasis gets but little further than this. Keyes,[6] quoting this statement, concludes that "a vesical tumor (carcinoma or sarcoma) remains confirmed to the bladder for years and rarely gives rise to metastases of any importance."

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[2] International Clinics. Philadelphia, 1894, 4th series, i, 231.

[3] Les tumeurs de la vessie. Paris, 1891.

[4] Traité des tumeurs de la vessie. Paris, 1895.

On the other hand, Albarran, in 16 observations, found glandular involvement 11 times, and Tuffier[7] in 15 autopsies found 3 instances of propogation to neighboring organs and 11 of glandular infection and generalization. Bland Sutton[8] testifies to the frequency of involvement of the pelvic lymph glands and of general dissemination.

An analysis of these and other conflicting statements seems to show that, generally speaking, clinicians hold to the view that vesical carcinomas tend to remain localized and form few metastases, although pathologists incline to a contrary opinion. Several factors may be responsible for this discrepancy: The nature of the lymphatic system of the bladder is such that a malignant tumor would naturally tend to remain localized in the earlier stages, which are more likely to fall under the observation of the surgeon than the pathologist. According to Poirier and Charpe, lymphatic vessels probably do not exist in the mucous membrane of the bladder, but the network of origin is intramuscular, from which the efferents lead into a second network between the muscularis and peritoneum or perivesical fascià. The neoplasms are said to originate most frequently in the deeper layers of the epithelium, and the direction of growth is at first naturally along the line of least resistance, toward the inner surface of the bladder. Another factor for this discrepancy is that without a postmortem examination there is a strong probability that metastases, especially in internal organs, will be overlooked. This statement might appear entirely superfluous, did not one meet with so many examples in the literature of attempts to draw conclusions from clinical observations alone. Another factor is the ease with which a benign may be mistaken for a malignant tumor. There are reports of considerable series of operations for the extirpation of "carcinoma of the bladder" with little or no reference to microscopic examinations.

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[5] Etat du systéme lymphatique dans les maladies de la vessie et de la prostate. Paris, 1898, Pp. 46, 52.

[6] The Surgical Diseases of the Genito-urinary Organs. New York, 1899, 259.

[7] Traité de Chirurgie. Paris, 1892, vii.

[8] Tumors, Innocent and Malignant. Philadelphia, 1893.

The following statement by Lincoln Davis[9] is apropos in this connection: "It is generally conceded that of two tumors which are macroscopically and microscopically indistinguishable, the bladder wall may show infiltration in one and not in the other." Finally, there is abundant evidence that benign tumors may undergo malignant transformation, and it might happen that the observer of the final stages had no knowledge of the long period that the tumor had manifested no signs of malignancy.

In 3 cases of our series no metastases or extravesical involvement was found; in 1 they are doubtful, none being described. In the other 6 cases metastases were present in various organs, as follows: four times each in the retroperitoneal glands and lungs; twice in bones, and once each in the peribronchial glands, inguinal glands, adrenal gland, kidney, and testicle.

The occurrence of metastases in the bones in 2 cases might lead to the suspicion of an error in diagnosis, especially as there is but little reference in the literature to such occurrences. However, the possibility of the tumors being sarcomas or prostatic carcinomas was excluded positively. The secondary tumors in the bones in these 2 cases entitle carcinoma of the bladder to a place in clinical medicine and surgery with the prostatic, adrenal, mammary, thyroid, and uterine tumors.[10]

A point deserving of special emphasis is the mode of death. In 7 of our cases this was due to ascending infection of the urinary tract. In each of the 7 cases there was demonstrable blocking of one or both ureters; in 3 by direct involvement and in 4 by pressure. The ureters in several instances were so dilated and their walls so hypertrophied that they resembled more the small intestine than the ureter.

Reference has already been made to the difficulty of diagnosis in primary carcinoma of the bladder. Probably in many cases the condition is not ascertained until postmortem examination. In our series the correct diagnosis was made in 2 cases from the symptoms and physical examination. In 2 other instances it was made after cystotomy for complications, while in 6 the primary tumor was unrecognized clinically.

The reasons for such mistakes, aside from the inherent difficulty of separating symptomatically the various affections of the bladder and contiguous structures, are two-fold. The first is the character of the complications which are especially prone to obscure the diagnosis in the later stages. The other is the character of the early symptoms. In the literature on this subject one meets with the oft-reiterated and much emphasized statements, that painless, copious, repeated, apparently causeless hematuria is a very early symptom; in the majority of cases the first observed by the patient, and that its character is not far from being pathognomonic. Yet in only 3 of these 10 cases was hematuria, sufficient to be noticed by the patient, an early symptom. One other patient observed blood in the urine in considerable amounts, but some time after the onset of pain and strangury. In the 5 remaining cases whose clinical history was obtainable hematuria was late, and only slight or microscopic in quantity. It would seem that there is no clinical symptom or combination of symptoms by which we can affirm or deny the presence of a vesical carcinoma, and that the only basis for a positive diagnosis is offered us by the cystoscope and the microscope.

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[9] Tumors of Urinary Bladder. Annals of Surgery, 1906, xliii, 556–591.

[10] See report by Yoder, Description of an Osteoplastic Metastatic Carcinoma of the Sternum Following a Primary Carcinoma of the Uterus. Med. News, December 6, 1902.

Conclusions. (1) Intelligent deductions and trustworthy statistics are to be derived only from careful and thorough study of a large number of cases from both the clinical and the anatomical sides. (2) The most frequent seat of carcinoma in the bladder and the direction of extension are still debatable questions. (3) Metastasis is much more frequent than is conceded by many clinicians. (4) A malignant growth in the bones may occur from a primary carcinoma of the urinary bladder. (5) The most frequent cause of death in vesical carcinoma is a secondary infection of the ascending urinary tract. (6) The diagnosis is always difficult, especially after the onset of complications.

INCOMPLETE AND COMPLETE HYPOTHYROIDŒA OR MYXŒDEMA.

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Deficient secretion of the thyroid, according to the degree of subactivity and age of the subject, may cause at least three distinct clinical entities. Deficiency of secretion varying in amount from nearly normal to virtually none may produce mild nervous symptoms of a vague nature, or various grades of *myxœdema, idiocy,* or *cretinism:* just as an excess of secretion, or hyperthyroidœa varying in degree produces either tachycardia or profound intoxication with severe derangement of the whole body, or even death. Somewhere, then, between the normal secretion and almost total cessation of secretion, producing marked and complete myxœdema, there is a condition of subsecretion which brings about what is known in medical parlance as incomplete hypothyroidœa or "*myxœdeme fruste.*" Cases of this nature are described in detail by Murray,[1] Hertoghe,[2] Ewald,[3] Richardson,[4] Moffitt,[5] and Howard,[6] and they

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[1] British Med. Jour., 1898; Twentieth Century Practice of Medicine.

[2] Nouv. Iconographe de la Saltpêtrière, 1899.

[3] Die Deutsche Klinik.

[4] The Thyroid and Parathyroid Glands, 1905.

[5] Jour. Amer. Med. Assoc., vol. xlv, No. 12.

Ibid., vol. xlviii, Nos. 14 and 16.